PATENT
ROSE 3.0-036 CIP IV

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re patent application of
Hiatt, et al

Serial No. 08/486,536

Filed: June 7, 1995

For: 3' PROTECTED NUCLEOTIDES FOR ENZYME CATALYZED TEMPLATE-INDEPENDENT CREATION OF PHOSPHODIESTER BONDS

Group Art Unit: 1211

Examiner: J. Wilson

Dated: August 12, 1997

RECEIVED
S 12/97

Assistant Commissioner For Patents
Washington, D.C. 20231

REQUEST FOR REINSTATEMENT

Sir:

Please note that on March 31, 1997, Applicants' new counsel filed a Revocation and Substitution of Attorneys with respect to the above-identified application, which has been entered. Applicants' previous attorneys received a Notice of Abandonment mailed March 18, 1997 for failure to respond to an Office letter mailed November 14, 1996. However, a response to said Office Action was mailed to the Patent and Trademark Office on December 13, 1996.

Attached hereto are copies of the Transmittal Letter, Supplemental Response to Office Action and a postcard indicating receipt in the Patent and

CERTIFICATION OF FACSIMILE TRANSMISSION

I hereby certify that this paper is being facsimile transmitted to the Patent and Trademark Office on the date shown below.

Peter J. Butch III, Esq.
Signature

8/12/97
Date

To: U.S.P.T.O.
Attn: Examiner J. Wilson
Fax No.: (703) 308-4556
No. of Pages: 14

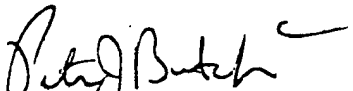
Trademark Office mailroom on December 16, 1996. Additionally, the documents bear a Certificate of Mailing dated December 13, 1996.

It is therefore believed that evidence has been submitted to establish that a response to the Office Action dated November 14, 1996 was timely filed, and is therefore respectfully requested that prosecution on the above-identified application be reopened.

If there are any fees due in connection with this communication, please charge same to our Deposit Account No. 12-1095.

Respectfully submitted,

LERNER, DAVID, LITTENBERG,
KRUMHOLZ & MENTLIK



PETER J. BUTCH, III
Reg. No. 32,203

600 South Avenue West
Westfield, New Jersey 07090
Telephone: (908) 654-5000
Facsimile: (908) 654-7866

F:\DOCS1\JODIL\3.0\96302.DOC

S.N. 08/486,536 Docket No. 214/177 Date Mailed 12/13/96 Atty. J. Guise
Title: 3' PROTECTED NUCLEOTIDES FOR ENZYME ... PHOSPHODIESTER BONDS
(Client Name) Rose-Hiatt Biotechnology

The Following, doc. in the U.S. Patent & Trademark Office, was received in the Patent & Trademark Office on the date stamped hereon:

___ Amendment
___ TM Appln., Including Specimens #
___ Application for Patent Including
___ Pages Spec.; No. of Claims
Declaration, Affidavit or Oath, Power of Attorney
___ Assign; Ck. No. ____ for $
___ Verified Statement
✓ Letter of Transmittal
___ Maintenance Fee Transmittal
___ Response to Office Action
___ Request for Extension of Time
___ Statement of Use, include specimens
___ Check No. ____ for $
Priority:

___ Drawings: # of Sheets
___ Formal ___ Informal
___ Issue Fee Transmittal
___ Power Re:
___ Notice of Appeal
___ Petition for
___ Advance soft copy order:
___ Ck. No. ____ for $
___ Certified Copy, #__ of Docs.
___ IDS
___ Express Mail #
✓ Supplemental Response to Office Action
___
___

900
12/11
12-16-97

214/177
Patent

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	Group Art Unit 1803
ANDREW C. HIATT and FLOYD ROSE	Examiner Wilson, J.
Serial No. 08/486,536	December 13, 1996
Filed: June 7, 1995	
For: 3' PROTECTED NUCLEOTIDES FOR ENZYME CATALYZED TEMPLATE-INDEPENDENT CREATION OF PHOSPHODIESTER BONDS	

TRANSMITTAL LETTER

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Transmitted herewith for filing in the above-referenced application are the following:

- Supplemental Response to Office Action; and

CERTIFICATE OF MAILING

I hereby certify that this paper (along with any referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

Jeanette M. Olivera
name of person mailing paper

December 13, 1996
date of deposit

Jeanette M. Olivera
signature of person mailing paper

SSSD/31375.v01

214/177
Patent

- Return postcard.

If there is any fee due in connection with this response, please charge our Deposit Account No. 12-2475 for the appropriate amount.

Respectfully submitted,

LYON & LYON

By _____
Jeffrey W. Guise
Reg. No. 34,613

First Interstate World Center
633 West Fifth Street, 47th Floor
Los Angeles, CA 90071-2066
(619) 552-8400

214/177
Patent

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	Group Art Unit 1803
ANDREW C. HIATT and FLOYD ROSE	Examiner Wilson, J.
Serial No. 08/486,536	December 13, 1996
Filed: June 7, 1995	
For: 3' PROTECTED NUCLEOTIDES FOR ENZYME CATALYZED TEMPLATE-INDEPENDENT CREATION OF PHOSPHODIESTER BONDS	

SUPPLEMENTAL RESPONSE TO OFFICE ACTION

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In response to the Office Action dated November 14, 1996, Applicants make the following clarifying amendments and repeat the arguments submitted in the original Office

CERTIFICATE OF MAILING

I hereby certify that this paper (along with any referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

Jeanette M. Olivera
name of person mailing paper

December 13, 1996
date of deposit

Jeanette M. Olivera
signature of person mailing paper

SSSD/31203.v01

214/177
Patent

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

ANDREW C. HIATT and FLOYD ROSE

Serial No. 08/486,536

Filed: June 7, 1995

For: 3' PROTECTED NUCLEOTIDES FOR ENZYME CATALYZED TEMPLATE-INDEPENDENT CREATION OF PHOSPHODIESTER BONDS

Group Art Unit 1803

Examiner Wilson, J.

December 13, 1996

SUPPLEMENTAL RESPONSE TO OFFICE ACTION

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In response to the Office Action dated November 14, 1996, Applicants make the following clarifying amendments and repeat the arguments submitted in the original Office

CERTIFICATE OF MAILING

I hereby certify that this paper (along with any referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

December 13, 1996
date of deposit

Jeanette M. Olivera
name of person mailing paper

Jeanette M. Olivera
signature of person mailing paper

SSSD/31203.v01

Action transmitted to the Patent Office on July 25, 1996. After conferring with Examiner James Wilson via telephone, it has been determined that in spite of the Applicants' specific instructions on the bottom of page 2 which direct the entry of various amendments to the claims, the amendment was not entered through no fault of the Applicant. Applicants believe that no fee is currently due. However if any such fees are due, Applicants authorize the fee to be charged to Deposit Account No. 12-2475.

AMENDMENT

Applicant respectfully requests that the following amendments to the claims be entered:

In the Claims

4. A nucleoside of 5'-phosphate of claim[s] 1, 2 or 3[-3] wherein said nucleoside contains a base selected from the group consisting of adenine (A), guanine (G), thymine (T), cytosine (c) and uracil (U).

5. A nucleoside 5'-phosphate of claim[s] 1, 2 or 3[-4] wherein said nucleoside 5'-phosphate is a nucleoside 5'-triphosphate.

6. A nucleoside 5'-phosphate of claim[s] 1, 2 or 3[-5] wherein said removable blocking moiety is enzymatically removable.

7. A nucleoside 5'-phosphate of claim 1, 2 or 3[6] wherein said removable blocking moiety is removed in under 10 minutes.

8. A nucleoside 5'-phosphate of claim[s] 1, 2 or 3[1-7] wherein said removable blocking moiety is linked to a solid support.

Remarks

The above-amendments to the claims were already presented in an Office Action filed on July 25, 1996, however, through no fault of the applicants the above-amendments were not entered and applicant received an Office Action mailed on November 14, 1996 informing applicants of this action. The applicants were given one month to submit a supplemental amendment and this submission satisfies that time limit. The remainder of this Office Action is identical to the action submitted on July 25, 1996.

1. Rejection of Claims 1-3 Under 35 U.S.C. § 112, first paragraph

Claims 1-3 of the instant application and the specification of the instant application have been rejected and objected to under 35 U.S.C. § 112, first paragraph, for failing to provide an adequate written description of the invention and failing to adequately teach how to make and/or use the invention. This rejection and objection is respectfully traversed.

Specifically, the examiner alleges that the specification and examples inadequately support the breadth of the claims, and that the applicant has failed to provide working examples and written description which teach how to make and use each of the MarKugh group members. Further, the examiner suggests that the specification does not teach the interchangeability of the various removable 3' protecting groups described by the specification.

It is respectfully submitted that the Federal Circuit has summarized the test for compliance with the "written description" requirement 35 U.S.C. §112:

> Although [the applicant] does not have to describe exactly the subject matter claimed, . . . the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed. [T]he test for sufficiency in supporting a patent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter."

Vas-Cath Inc. V. Mahurkar, 935 F.2d 1555, 1562 (Fed. Cir. 1991) (quoting In Re Gosteli, 872 F.2d 1008, 1012 (Fed. Cir. 1989). From this quote the examiner can readily see that the Federal Circuit does not require verbatim disclosure of what is claimed for compliance with the written description requirement. Rather,

> [I]f a person of ordinary skill in the art would have understood that the inventor had been in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate written description requirement is met.

In re Alton Inc., 76 F.3d 1168, 1175 (Fed. Cir. 1996). It is also clear that, because a claim is broader than a specific embodiment disclosed in the specification, patentability is not adversely affected. Ralston Purina Co. v. Far-Mar-Co Inc., 772 F.2d 1570, 1575 (Fed. Cir. 1985).

It is further submitted that the specification need only enable one of ordinary skill in the art to practice the invention without undue experimentation. (In re Stephens, 529 F.2d 1343 (C.C.P.A. 1976) Simply put, the specification must teach a skilled artisan how to make and use the invention based on the specification and the knowledge possessed by one of skill in the art.

It is respectfully submitted that the instant specification fulfills both the written description and enablement requirements of 35 U.S.C. §112. The specification at page 13, lines 7-13 fully define a removable blocking moiety as

> "a removable blocking moiety is a moiety which is attached to the oxygen at the 3' position of the nucleoside, or equivalent position in a nucleoside analog. The removable blocking moiety prevents the reaction of the 3' oxygen when present and is removable under deblocking conditions so that the 3' oxygen can then participate in a chemical reaction."

Further, at page 31, lines 35 to page 33, lines 34, the specific deblocking conditions and properties of various removable blocking moieties are described. Further, this section also indicates that one of ordinary skill in the art given the particular requirements of the removable 3' blocking moiety would let the blocking moiety be removed in under ten minutes to produce the hydroxy group at the 3' position so that the 3' hydroxyl is available for reaction. (Page 28, lines 9-15.) The specification also discloses a broad range of compounds which will act as removable 3' blocking moieties at page 18, line 26-page 28, line 15.

In light of the disclosure of the properties of the removable blocking moiety and the compounds disclosed, one of skill in the art would understand the parameters required for a compound to be useful in this invention. It is respectfully submitted that this disclosure clearly enables one of skill in the art to make and use the present invention without undue experimentation. Further, the disclosed compounds in the specification at pages 18, lines 26 to page 28, line 15 clearly indicate to one of skill in the art that the present inventors were in possession of those compounds at the time of filing the instant application.

It is respectfully submitted that in light of the clearly sufficient disclosure which enables one of skill in the art to make and use the claimed compounds, the enablement rejection fails under the appropriate legal standards. It is further submitted, that the disclosure in the specification of the specific compounds useful as removable 3' blocking moieties clearly indicates the applicant contemplated at least those compounds at the time of filing. Therefore, it is respectfully requested that this rejection be withdrawn.

2. Rejection of Claims 1-3 Under 35 U.S.C. § 103

Claims 1-3 have been rejected under 35 U.S.C. § 103 as being unpatentable over the Andrus et al. patent no. 4,816,573, the Cruickshank patent no. 5,091,519 and the Bennett et al., Biochemistry, Vol. 12, No. 20, pgs. 3956-3960 (1973) article and the Kaufmann et al., Eur. J. Biochem., Vol. 24, No. 1, pgs. 4-11 (1971). Specifically, the examiner states that the Andrus patent discloses capping of the 3'-hydroxyl position of a nucleotide which renders the instant claims drawn to removal of blocking groups at the 3'-hydroxyl position obvious. The applicants respectfully traverse this rejection.

The examiner specifically rejected the instant claims based on column 2, lines 67-68 of the Andrus patent which read as follows:

> As used herein, the term capping refers to reacting either the free 5' hydroxyl of a 3' to 5' growing nucleotide chain or the free 3' hydroxyl of a 5' to 3' growing nucleotide chain with a capping agent to render the chain incapable of participating in subsequent condensation steps. The preferable capping agents of the invention are phosphite monoesters of the form... (emphasis added)

This particular portion of the Andrus patent is consistent with the invention disclosed by the remainder of the Andrus patent and is directed to "capping agents". These capping agents render the nucleotide chain incapable of participating in subsequent condensation steps. This is in direct contrast to the removable blocking groups identified in the instant application and claims. These removable blocking groups specifically allow for their attachment and subsequent removal as required by the present invention.

It is respectfully submitted that the disclosure of capping agents which "render the chain incapable of participating in subsequent condensation steps" does not render obvious the instant removable blocking groups. The Andrus patent itself does not provide any motivation for one of skill in the art to utilize any of the disclosed chemical protecting groups as removable blocking groups in the manner of the present invention and does not describe any removable blocking group. Therefore it is respectfully submitted that the Andrus patent cannot be successfully combined with any other reference to result in the present invention or render the present invention obvious.

The examiner has also cited the Bennett et al. reference as disclosing 3'-methoxyethyl protecting groups for the 3'-position of a 5'-phosphate nucleoside compound. Specifically, the examiner cites to page 3956, column 2 and formula I of figure 1 on page 3957. The Bennett et al. reference discloses 5'-diphosphates and does not specifically discuss or disclose any 5'-nucleotide triphosphates. The specific citations to the Bennett et al. Reference cited by the examiner do not disclose triphosphates but rather are focused on adenosine 5'-diphosphate. It

is respectfully submitted that the Bennett reference does not address or disclose 5'-triphosphates in blocking moieties which may be useful with 5'-triphosphates.

The examiner has also cited Kaufmann et al. as disclosing 3'-O-isovaleryl nucleoside diphosphates. Specifically the examiner refers to page 5 of the Kaufmann article as disclosing these particular nucleotide diphosphates. Again, it is respectfully pointed out that the Kaufmann reference refers only to diphosphates and does not discuss or disclose the use of any particular blocking groups with 5'-nucleoside triphosphates.

The examiner cites the Cruickshank patent as teaching as teaching the attachment of removable blocking groups to nucleotides containing linking groups for use as non-isotopic labels. Specifically, column 14 of the Cruickshank patent is cited as disclosing a nucleotide having an acetyl or phosphoramidite moiety at the 3'-position. The examiner further asserts that the variable x in the formula shown in column 14 when replaced with a triphosphate renders the instant claims obvious. The examiner further states, without providing any specific reference, that the Cruickshank patent teaches the interchangeability of the mono-, di- and triphosphate moieties.

It is respectfully pointed out that the Cruickshank patent does not teach the use of blocking groups independent from the nucleosides containing the linking groups. The Cruickshank patent does not provide any explanation or use or disclosure of nucleosides having the shown blocking groups independent from the linking groups attached to the disclosed nucleotides. It is respectfully submitted that the Cruickshank patent fails to render

obvious to one of skill in the art the use of the blocking groups independent from the concurrent use of the various linking groups disclosed. Further there is no suggestion in the Cruickshank patent that any use of nucleotides not containing a linking group is contemplated.

In light of the above discussion, the Andrus and Cruickshank patents together with the Bennett and Kaufmann articles do not provide a disclosure which, taken separately or together, renders obvious the presently claimed invention. These patents and references fail to disclose the use of a removable blocking group at the 3'-carbon of a nucleoside 5'-triphosphate as required by the claims. Further, the cited references do not suggest to one of skill in the art to utilize the blocking groups independently from the nucleosides containing the linking groups disclosed in the references. It is respectfully submitted that without specific motivation to independently use the portions of the cited compounds identified by the examiner, the examiner is inappropriately using hindsight to reconstruct the instant invention. It is therefore respectfully requested that the examiner withdraw this rejection to claims 1-3.